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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,446	04/22/2005	Christoph De Haen	B-0497 PUS	1688

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BRACCO RESEARCH USA INC.
305- COLLEGE ROAD EAST
PRINCETON, NJ 08540

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,446	DE HAEN ET AL.	
	Examiner	Art Unit	
	BRANDON J. FETTEROLF	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/2005; 1/16/2007; 10/15/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Exhibit I*.

DETAILED ACTION

Election/Restrictions

The Election filed on 1/22/2008 in response to the Restriction Requirement of 9/20/2007 has been entered. Applicant's election of Group II, claims 10-16, as specifically drawn to the special technical feature of a process for the preparation of a conjugate has been acknowledged. Applicants have further elected the species of Example 4, in which the Fab fragment is anti-Herpes simple virus, the conjugation moieties are compound D of Example 2, final compound is a di-conjugate and the conditions used are those of pending claim 16. Thus, the election has been treated as an election without traverse because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement (MPEP § 818.03(a)).

The restriction requirement is therefore deemed to be proper and is made FINAL.

(Note: As stated above, Applicants election of the species of Example 4 is acknowledged. However, while the Examiner appreciates Applicants election of a species, the previous restriction requirement did not require an election of species. As such, the election of species is moot.)

Claims 1-22 are currently pending.

Claims 1-9 and 17-22 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 10-16 are currently under consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The Information Disclosure Statement filed on 4/22/2005 and 10/15/2005 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The information disclosure statement filed on 1/16/2007 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show the migration as described in the specification (page 18, lines 19+). Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet,

and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 11 recites the broad recitation a phosphine, and the claim also recites tributylphosphine and tris-(carboxyethyl)-phosphine which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (WO 91/04056 A1, 1991, IDS).

Hansen et al. teach a method for "instant" labeling of monovalent, e.g., Fab or Fab', antibody fragments containing at least one and preferably a plurality or spatially adjacent stabilized free sulfhydryl groups (page 3, lines 3-6). For example, the WO document teaches that a Tc-99m-labeled fragment can be made via (i) reducing a Fab fragment such as anti-CEA to Fab-SH with cysteine and (ii) adding sodium pertechnetate and stabilized stannous ions (page 9 to page 10, Example 1). Moreover, the WO document teaches that the resultant Tc-99m-radiolabeled antibody fragments are suitable, and in fact particularly convenient and efficacious, in methods of non-invasive scintigraphic imaging of tumors and lesions (column 8, lines 3-7).

Claims 10-13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Maurer et al. (WO 02/056907 A2, IDS) as evidenced by Cruse and Lewis (Cruse, Julius and Lewis, Robert. Illustrated Dictionary of Immunology Boca Raton, FL, 1995).

Maurer et al. teach a method of coupling Fab fragments to Qβ capsid proteins comprising combining a first solution of a reduced fab fragment generated by reacting a concentration of a Fab fragment, 2.5 mg/mL, at a pH of 7.2 with different concentration (0-1000mM) of either dithiothreitol (DTT) or tricarboxyethylphosphine (TCEP) for 30 minutes at 25°C and a second solution comprising a SMPH derivatized Qβ capsid protein, wherein the final concentration of the protein and Fab were 1.14 mg/mL and 1.78 mg/mL respectively and the reaction proceeded overnight at 25°C (pages 140-141, Example 16). Thus, while Maurer et al. do not explicitly report the Fab concentration in μM or the conjugating moiety concentration in mM, e.g., micromoles/microliter or millimoles/mL, the concentration of the Fab will depend on its molecular weight reported in g/mol which as

evidenced by Cruse and Lewis is 47,000 KD, e.g., 47,0000 g/mol (Definition of Fab fragment). Thus, the μM concentration used by the prior art reference is 53μM (See Exhibit I for conversion).

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurer et al. (WO 02/056907 A2, IDS) as evidenced by Cruse and Lewis (Cruse, Julius and Lewis, Robert. Illustrated Dictionary of Immunology Boca Raton, FL, 1995).

Maurer et al. teach a method of coupling Fab fragments to Qβ capsid proteins comprising combining a first solution of a reduced fab fragment generated by reacting a concentration of a Fab fragment, 2.5 mg/mL, at a pH of 7.2 with different concentration (0-1000mM) of either dithiothreitol (DTT) or tricarboxyethylphosphine (TCEP) for 30 minutes at 25°C and a second solution comprising a SMPH derivatized Qβ capsid protein, wherein the final concentration of the protein and Fab were 1.14 mg/mL and 1.78 mg/mL respectively and the reaction proceeded overnight at 25°C (pages 140-141, Example 16). Thus, while Maurer et al. do not explicitly report the Fab concentration in μM or the conjugating moiety concentration in mM, e.g., micromoles/microliter or millimoles/mL, the concentration of the Fab will depend on its molecular weight reported in g/mol which as evidenced by Cruse and Lewis is 47,000 KD, e.g., 47,0000 g/mol. Thus, the μM concentration used by the prior art reference is 53μM (See Exhibit I for conversion).

Maurer et al. does not explicitly teach that the Fab concentration is from 1.5-10 μM or 1-5 μM. Nor does Maurer et al. explicitly teach that the conjugate moiety concentration is 0.1-100 mM.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to optimize the concentration of the Fab fragment and

resultant conjugate moiety because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by optimizing the concentration of the Fab fragment and resultant conjugate moiety, one would achieve the optimal reaction conditions for the conjugation.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Primary Examiner
Art Unit 1642

/Brandon J Fetterolf, PhD/
Primary Examiner, Art Unit 1642